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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
SEHARASEYON, JEGATHEESAN

ART UNIT	PAPER NUMBER
1647	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/760,810	OLMARKER ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5 & 9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This office action is response to Applicant's election of TNF-α inhibitor which is a metalloproteinase inhibitor excluding methylprenisolone. Election was made with traverse in Paper No. 12 (4/26/02). The traversal is on the ground(s) that the search of all claims would not impose a serious burden on the Office. This is not found to be persuasive because the search for a single TNF-α inhibitor will not automatically lead to the identification other TNF-α inhibitors. Therefore, the searches for each of the inhibitors are not coextensive and would be a burden on the office to search all of the inhibitors. Therefore, the restriction requirement is deemed proper and made FINAL.

2.The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27, 28, 31,32, 35, 36, 39, 40, 43, 44, 47 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3a. Claims 27, 28, 31,32, 35, 36, 39, 40, 43, 44, 47 and 48 recite the limitation "pharmaceutical composition of claim 22". However, claim 22 is drawn to a method. Therefore, there is insufficient antecedent basis for this limitation in the claim. For the purpose of further examination, the Office will consider the pharmaceutical composition

to contain TNF-α inhibitors excluding methylprenisolone as per the election species. Claims 31,32, 35, 36, 39, 40, 43, 44, 47 and 48 are rejected insofar as they depend on rejected claims 27 and 28.

3b. Claims 2, 26,29, 30, 33, 34, 37, 38, 41, 42, 45 and 46 are rejected as being vague and indefinite in the recitation of the term "pharmaceutically effective amount ". It is unclear what pharmaceutically effective amount is encompassed in the instant claim. Since the instant claim also includes several nerve disorders this effective amount could vary depending on the nerve disorder. Claims 26,29, 30, 33, 34, 37, 38, 41, 42, 45 and 46 are rejected insofar as it depends on rejected claim 2.

3c. Claims 27, 28, 31,32, 35, 36, 39, 40, 43, 44, 47 and 48 provide for the use of pharmaceutical compositions, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4a. Claims 27, 28, 31,32, 35, 36, 39, 40, 43, 44, 47 and 48 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps

involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claims 1-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of nucleus pulposus-induced nerve root injury, does not reasonably provide enablement for treating nerve disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the

existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification as filed is insufficient to enable one skilled in the art to practice the claimed invention without an undue amount of experimentation. Nerve disorders have several etiologies. Applicants have demonstrated that by using antibody to TNF-α or deoxycycline are able to treat nucleus pulposus-induced nerve root injury by inhibiting TNF-α (Page: 13, lines 6-13). Thus, it appears that the applicants are enabled to treat specific nerve injuries, which results in the liberation of TNF-α. It is unclear if the disclosed studies are adequate to represent the treatment regiment for all nerve disorders with other etiologies. In addition, there is no guidance provided in choosing the effective amount for administering to the subjects to treat the various nerve disorders. Applicants recites a broad, arbitrary, range with no evidence of the amount necessary to achieve the desired effect. Since applicant has not provided any working examples of the efficacy of treating already established disease subjects or applicable model of nerve disorders with TNF-α inhibitors, it would require an undue amount of experimentation to one of skill in the art to practice the claimed invention.
Given the breadth of claims 1 and 2 in light of the unpredictability of the art as determined by the lack of working examples, the level of skill of the artisan, and the lack of guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention to treat all nerve disorders using the TNF-α inhibitors. Claims 3-48 are rejected insofar as they depend on rejected claims 1 and 2.

5b. Claims 1-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

Applicants have described nucleus pulposus-induced nerve root injury in pigs (pages 5-9) and the treatment of this injury using TNF-α inhibitors. The specification does not disclose all nerve disorders to be treated by inhibiting TNF-α. The claims as written, however, encompass the treatment of all nerve disorders by administering TNF-α inhibitors in mammals which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 1 and 2. The specification does not provide written description for all nerve disorders. *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*See Vas-Cath* at page 1116). Applicant is reminded that

Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

With the exception of treating nucleus pulposus-induced nerve root injury by inhibiting TNF-α, applicants have not described that by using antibody to TNF-α or deoxycycline are able to treat all nerve disorders by inhibiting TNF-α. Thus, the skilled artisan cannot envision all the contemplated nerve disorders, regardless of the complexity or simplicity of the disorders and the treatments. As a result, it does not appear that the inventors were in possession of invention to treat all nerve disorders as set forth in claims 1 and 2. Claims 3- 48 are rejected insofar as they depend on rejected claims 1 and 2.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6a. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Sommer et al. (1997).

The instant invention is directed to treatment of a nerve disorder by inhibiting TNF-α using metalloproteinase inhibitor.

Sommer et al. teaches the use of metalloproteinase inhibitor TAPI to block the mature TNF (abstract). The pharmacological inhibition of TNF production by TAPI

reduces pain related behaviors in mice with chronic constriction injury (CCI). Therefore, the disclosure of Sommer et al. anticipates claim 1. Claims 1, 3-25, 27, 28, 31, 32, 35, 36, 39, 43, 44, 47 and 48 are rejected insofar it depends on rejected claim 1.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7a. Claims 1-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sommer et al. (1997) in view of Xue et al. (U. S. Patent No. 5,703,092).

The instant invention is directed to treatment of a nerve disorder by inhibiting TNF-α by administering of metalloproteinase inhibitor (TNF-α inhibitor).

The relevance of Sommer et al. has been set forth above. However, Sommer et al. do not explicitly recite the administration of TNF-α inhibitor containing

pharmaceutical to a human. They also do not disclose the administration of the inhibitor systemically, orally or intramuscularly.

Xue et al. discloses the identification of a metalloproteinase inhibitor which inhibits the production TNF and thus is useful for the treatment of various diseases including inflammatory conditions (abstract). In addition, they discuss pharmaceutical composition suitable for administration (column 41, lines 23-28). Furthermore, they also discuss the treatment of humans and various forms of administration including oral and intramuscular delivery (column 39, line 44 to column 40, line 33). Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made to modify the methods disclosed in Sommer et al. to treat neurological conditions as described in Xue et al. One of ordinary skill in the art would have been motivated with reasonable expectation of success to modify the methods of Sommer et al. because Xue et al. teaches the treatment using pharmaceutical compositions containing metalloproteinase inhibitor and the various forms of administration into mammals including humans to inhibit the production of TNF to treat inflammation. Therefore, the instant invention is obvious over Sommer et al. (1997) in view of Xue et al. (U. S. Patent No. 5,703,092).

6b. Claims 1-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (1996) in view of Xue et al. (U. S. Patent No. 5,703,092).

Wang et al. teaches the production of TNF in spinal cord following traumatic injury in rats. Further they demonstrate that TNF production is an acute and

rapid reaction in the spinal cord following traumatic injury (abstract). However, Wang et al. do not explicitly recite the administration of TNF-α inhibitor to a mammal to inhibit the TNF production and to treat nerve injury. They also do not disclose the administration of the inhibitor in a pharmaceutical composition systemically, orally or intramuscularly.

Xue et al. discloses the identification of a metalloproteinase inhibitor which inhibits the production TNF and thus is useful for the treatment of various diseases including inflammatory conditions (abstract). In addition, they discuss pharmaceutical compositions suitable for administration (column 41, lines 23-28). Furthermore, they also discuss the treatment of humans and various forms of administration including oral and intramuscular delivery (column 39, line 44 to column 40, line 33). Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made to modify the methods disclosed in Wang et al. to treat neurological conditions resulting from the spinal cord injury by inhibiting TNF as described in Xue et al. One of ordinary skill in the art would have been motivated with reasonable expectation of success to modify the methods of Wang et al. because Xue et al. teaches the treatment using pharmaceutical compositions containing metalloproteinase inhibitor and the various forms of administration into mammal including humans to inhibit the production of TNF to treat inflammation. Therefore, the instant invention is obvious over Wang et al. (1996) in view of Xue et al. (U. S. Patent No. 5,703,092).

7. No claims are allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and 703-308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JS
May 17, 2002

JEFFREY STUCKER
PRIMARY EXAMINER